REMARKS

The specification has been amended to provide updated information.

Claims 1-18 were pending when last examined. Claims 1, 17 and 18 have been amended. Claims 6 and 12 have been canceled. Claims 19 and 20 are newly added.

Claim Rejections under 35 USC § 102

Claims 1-12 are rejected under 35 USC § 102(b) as being anticipated by the article titled "Work in Progress: 252Cf Neutron Brachytherapy for Hemispheric Malignant Glioma" by Maruyama et al. ("Maruyama").

Claims 1 and 7 are patentable over Maruyama at least because they recite "inserting ... miniaturized concentrated neutron emitting source into [a] tumor ... wherein ... the neutron emitting source[(s)] has an outer diameter that is about 2 mm or less and about 100 μg or more of californium-252."

While implanting a neutron-emitting source to treat tumors has been under investigation for some time, the utility of these methods have been limited thus far by the restrictive concentration density range of neutron sources such as ^{252}Cf. Because the concentrations of the implantable neutron-emitting sources have thus far been low, they were only effective for treatment of tumors in large, accessible body cavities that allow insertion of large enough neutron source. For smaller body parts into which only smaller neutron sources can be inserted, the dosage of the neutron source could not be made high enough for a successful treatment. The invention vastly expands the utility of neutron brachytherapy by employing a *miniaturized* (i.e., outer diameter of less than about 2 mm) and *concentrated* (i.e., having about 100 μg or more of californium-252 while having an outer diameter of less than about 2 mm) ^{252}Cf source that provides the medical practitioner with a method for treating tumors that is highly efficacious even for body parts that are too small to be treated with the conventional neutron source.

Maruyama does not disclose or suggest using a "miniature concentrated" neutron emitting source. In fact, Maruyama teaches away from using the neutron emitting source of the concentration range recited in Claim 1 because he describes an attempt to treat brain tumor by supplementing the neutron treatment with "whole brain photon therapy up to 6,000 rad (60 Gy) over a five-week to seven-week period using fractionated radiotherapy." This type of prolonged

supplemental photon therapy would not be necessary with the neutron treatment of the sort described in Claim 1. Effectively, Maruyama teaches to use a supplemental treatment with neutron brachytherapy using a low-concentration neutron source rather than employing a neutron-emitting source of a higher concentration than what is generally used. Since Maruyama does not disclose a neutron emitting source that has "a diameter that is about 2 mm or less and 100 μg or more of californium-252," Claim 1 is patentable over Maruyama.

Claims 2-6 and 8-12 depend from Claims 1 and 7 and are therefore patentable over Maruyama for the same reasons as Claims 1 and 7.

Claim Rejections under 35 USC § 103

1. Rejections of Claims 13-17

Claims 13-17 are rejected under 35 USC § 103(a) as being unpatentable over Maruyama in view of the article titled "Measurement of augmentation of ^{252}Cf Implant by ^{10}B and ^{157}Gd Neutron Capture" by Wierzbicki et al. ("Wierzbicki").

Claims 13-17 are patentable over a combination of Maruyama and Wierzbicki at least because it recites that "...the neutron emitting source has a diameter of about 2 mm or less and about 100 μg or more of californium-252." As stated above, Maruyama does not teach or suggest the recited concentration of californium-252. Wierzbicki, likewise, does not mention using the californium-252 concentration of the ranges recited in Claims 13-17. Rather, Wierzbicki describes pilot experiments performed "for a typical (idealized) arrangement of 19 μg ^{252}Cf sources used in brain implants" (p.789). Even assuming, *arguendo*, that Wierzbicki's source lies within the diameter range recited in Claims 13-17, 19 μg lies outside the recited range of "100 μg or more of californium-252." The inventions of Claims 13-17 are based on the recognition that neutron californium brachytherapy may be successfully performed using a miniaturized and concentrated neutron emitting source but neither Maruyama nor Wierzbicki discusses this type of neutron emitting source.

2. Rejection of Claim 18

Claim 18 is rejected under 35 USC § 103(a) as being unpatentable over Maruyama in view of the article titled "The Development of Californium-252 Sealed Sources at the Commissariat A L'Energie Atomique" by Barthelemy, et al. ("Barthelemy"). The rejection is based on an assertion

that Maruyama teaches all the limitations of claim 18 except for the exact size of the source. More specifically, the rejection states that "In Figure 13 of page 212, Barthelemy et al teach that the capsule of the source has an outside diameter of 0.70 mm and a length of 4 mm. Further, Barthelemy et al teach that the source is nominally 32" *See* Page 3, Office Action of September 21, 2004.

Claim 18 is patentable over Maruyama and Barthelemy because it recites that its "neutron emitting source is 3 – 6 mm in length, has an outside diameter of .50 -2 mm, and contains between 100μg and 1 mg of californium-252." First, Barthelemy does not disclose the neutron source that is described in Claim 18. Applicants respectfully submit that this rejection is based on a misreading of Barthelemy's Figure 3. Although Barthelemy's Figure 13 mentions the dimensions of 0.70 mm outside diameter and 4 mm length, these dimensions do not refer to the neutron source; rather, they refer to the Pt capsule. The only reference to californium-252 in Figure 13 is that its weight is 0.32 μg (*not* 32 μg as stated in the Office Action). 0.32 μg lies outside the weight range of "100 μg or more of californium-252" recited in Claim 18.

Second, Applicants respectfully submit that the difference between Maruyama-and-Barthelemy and Claim 18 is more than a mere "change in proportion." The neutron-emitting source of the invention is californium-252 of an entirely different concentration density than what is used in Maruyama or Barthelemy. The fact that about 100 μg or more of californium-252 can be packed into a size as small as "3 – 6 mm in length [and] an outside diameter of .50 -2 mm" opens up new possibilities for californium-252, such as treatment of tumors in areas that were previously difficult to access for neutron brachytherapy.

The rejections also state that there are other sources, as shown in Table III of page 207, which contain 100-500 μg of californium-252, and that a change in proportion is generally recognized as being within the level of ordinary skill in the art. However, Barthelemy clearly indicates that the neutron sources of Table III are for industrial applications. Barthelemy describes medical applications in a separate section of the article and makes it clear that the neutron sources for the two types of applications are processed differently (pp.202-203). Barthelemy does not suggest that it would be appropriate to use the industrial neutron sources for medical applications. Furthermore, the smallest source described in Table III for industrial applications contains a maximum californium-252 load of 100 μg is indicated to have an outside diameter of 8 mm, which is outside the diameter range recited in Claim 18.

For the foregoing reasons, Claim 18 is patentable over a combination of Maruyama and Barthelemy.

Claim Rejections – Obviousness-type Double Patenting

Claims 1-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-18 of U.S. Patent No. 6,685,619. A terminal disclaimer filed herewith overcomes the double patenting rejections.

New Claims

Claims 19 and 20 are newly added. These claims depend from Claim 1 and 7, respectively, and are patentable for the same reasons as Claims 1 and 7. The small size of the neutron emitting source employed in the invention allows insertion of more than one source into the tumor area, thus increasing the effective localized dose of radiation and reducing the necessary exposure time.

Conclusion

Based on the foregoing reasons, Claims 1-5, 7-11, and 13-20 are in condition for allowance. Please telephone the undersigned attorney at (650) 833-2121 if there are any questions.

Respectfully submitted,

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